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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,796	11/15/2001	Avi J. Ashkenazi	P3130R1C1	5287

7590 05/06/2005

Attn: Ginger R. Dreger, Esq.
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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 05/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,796	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-47 and 50-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-47 and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 24, 2005 has been entered.

2. Claims 40-47 and 50-52 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on January 24, 2005 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

6. Claims 40-47 and 50-52 stand rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for those reasons of record in previous office actions of record as directed to the previously presented limitations.

Applicant traverses the rejection by first reviewing case law pertinent to the utility requirement and refers to Utility Examination Guidelines (pages 5-6 of the Response). Applicant

further submits that the claimed PRO444 polypeptides are useful because they "induce the expression of c-fos in pericyte cells and, therefore, are useful not only as diagnostic markers for pericyte associated tumors, but also for giving rise to antagonists that are useful for the therapeutic treatment of pericyte associated tumors", and also, "as c-fos expression indices angiogenesis, the third asserted utility is that PRO444 polypeptides are useful in stimulating angiogenesis" (middle at page 7 of the Response). Applicant's arguments have been carefully considered but are not deemed to be persuasive for the following reasons.

A specification can meet the legal requirements of utility and enablement for a new polypeptide as long as the specification discloses at least one credible, specific and substantial asserted utility for the new polypeptide, or a well-established utility for the claimed polypeptide would be immediately obvious to the skilled artisan. A hypothetical example may serve to clarify. For example, a hypothetical specification discloses that a claimed polypeptide is expressed in colon cancer and not expressed in healthy colon tissue. The hypothetical specification does not disclose the biological activity of the polypeptide. The polypeptide in the hypothetical example would not be rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as it has utility and is enabled as a colon cancer marker. However, such is not the fact pattern here. The instant specification discloses in the Example 60 that PRO444 polypeptide of SEQ ID NO: 9 induced the expression of c-fos in pericyte cells (page 142, Example 60). There appears to be no disclosure that PRO444 polypeptides are exclusively present or expressed at the altered levels in pericyte-associated tumors. Thus, PRO444 polypeptides cannot be used as markers for pericyte-associated tumors and, therefore, this asserted utility is not specific. Further, as fully explained in the previous communications of record, there appears to be no factual evidence or scientific

reasoning to support a conclusion that PRO444-induced activation of expression of c-fos is specifically related to pericyte associated tumors or to angiogenesis.

The Declaration of Dr. Mary Gerritsen (The Gerritsen Declaration) under 37 CFR 1.132 filed January 24, 2005 is insufficient to overcome the rejection of claims 40-47 and 50-52 based upon lack of utility under 35 U.S.C. §§ 101 and 112, first paragraph as set forth in the last Office action for the following reasons.

The Gerritsen Declaration explains that retinal pericytes used in Assay 93 of Example 60 are important in regulating angiogenesis (paragraph 6 of the Declaration) and "c-fos is a transcription factor involved in the regulation of cellular growth, including cancer and angiogenesis". Therefore, "[i]n light of their significant relationship with angiogenesis and cancer, it is useful to identify compounds capable of stimulating pericytes through the c-fos pathway in order to treat, promote and diagnose these conditions" (paragraph 7 of the Declaration).

First, it is important to point out that reasoning presented in paragraphs 6 and 7 of The Declaration of Gerritsen represents only Dr. Gerritsen's own conclusions with no references to scientific publications so that the Examiner can make an independent analysis of the available information (see *Meitzner v. Mindick,* 549 F.2d. 775, 782, 193 USPQ 17, 22 (CCPA 1977), "Argument of counsel cannot take the place of evidence lacking in the record"). As such, there appears to be no evidence presented in the instant specification, as filed, or published scientific data that would allow to correlate or specifically connect induction of c-fos expression with cancer or angiogenesis, as asserted in Applicant's Response or in The Gerritsen Declaration. The art clearly recognizes that induction of c-fos can be evoked by a variety of extracellular stimuli,

that it represents the first line of cellular response which does not require synthesis of proteins and which can be regulated at different intracellular levels (see, for example, Coulon et al., J. Biol. Chem., 1999, Vol. 274, No. 43, pp. 30439-46, abstract and page 304439 especially).

Further, as correctly pointed out in the Declaration of Gerritsen, many growth factors are capable to stimulate growth of pericytes through activation of c-fos pathway (paragraph 6 of the Declaration). See, for example, article by Sakurai et al. (Sakurai et al., Invest. Ophthalmology and Visual Sci., 2002, Vol. 43, No. 8, pp. 2774-81), which describes c-fos activation in pericytes treated with prostaglandins, and Otani et al. (Otani et al., Invest. Ophthalmology and Visual Sci., 2000, Vol. 41, No. 5, pp. 1192-1199), which teaches pericytic c-fos activation caused by angiotensin II and VEGF. Again, in the instant case there appears to be no specific biological function that could be particularly attributed to PRO444 with respect to its ability to activate c-fos expression in pericytes.

Also, it is stated in the article published in 2003 by Ozerdem et al. (Ozerdem et al., Angiogenesis, 2003, 6, pp. 241-249), that although pericytes play important role in angiogenesis, their role in formation of tumor neovasculature is currently not fully understood and varies depending on type of tissue and tumor (see page 241, 242 and 246). Therefore, according to the current state of the art, induction of c-fos expression by PRO444 cannot be specifically associated with "onset of cancer and/or angiogenesis", as asserted in the Gerritsen Declaration (paragraph 7).

At paragraph 8 of the Declaration, Dr. Gerritsen submits that activation of c-fos was specifically attributed to PRO444 because in Assay 93 both positive and negative controls were present. The Examiner does not dispute the correctness of the experimental protocol. It was

never argued by the Examiner that there are factors that do not evoke induction of c-fos activation. However, there appears to be no clear physiological meaning attributed to the activation of c-fos by PRO444 at the time of filing. Therefore, the fact that out of 646 samples of different factors PRO444 polypeptide was among 48, which were able to induce c-fos expression in pericytes (paragraph 10 of the Declaration), does not, alone, provide for practical utility of the claimed polypeptides. It is a matter of law that the claimed invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. In the instant case, one skilled in the art would have to perform a significant amount of further experimentation in order to be able to use the instant claimed polypeptides for diagnosis or treatment of cancer or for any other asserted use.

With respect to the issue of activation of c-fos and cell specificity, which was brought in paragraph 9 of the Declaration, cited earlier article by Coulon et al. clearly indicates that not only nervous cells but cells of different types response to "wide range of extracellular stimuli" by activation of immediate early response gene *c-fos* (see abstract and page 30439, for example).

Therefore, for reasons of record presented in the previous office actions and reasons fully explained above, the instant rejection of claims 40-47 and 50-52 is maintained.

Claim Rejections - 35 USC § 112

7. Claims 40-47 and 50-52 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 40-44 and 51-52 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for those reasons of record as clearly explained in the previous office actions of record.

Applicant traverses the rejection on the premises that "skilled practitioners in the art could run a polypeptide having the claimed structure through an assay similar to Assay 93 (disclosed in Example 60 on page 142 of the specification) to determine whether the polypeptide in question was able to induce c-fos expression" (top at page 12 of the Response). This argument has been fully considered but is not persuasive because the instant claims are rejected under 35 U.S.C. 112, first paragraph, lack of written description of the claimed subject matter, which is severable from its enablement provision. In the instant case, the instant specification fails to describe in a written form the claimed molecular embodiments. While this is true that a skilled in the art can easily determine if a polypeptide induces c-fos activation in pericytes by testing it as disclosed in Assay 93, this is not a probative measure to satisfy the provision of written description requirement under 35 U.S.C. 112, first paragraph. It is not the ability of one skilled in the art to make and test if a compound meets the structural and functional limitations of the claims but rather the specification, which must clearly describe the claimed compounds. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Conclusion

9. No claim is allowed.

10. This is a continuation of applicant's earlier Application No. 10/002,796. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1646

March 11, 2005